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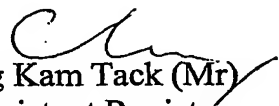
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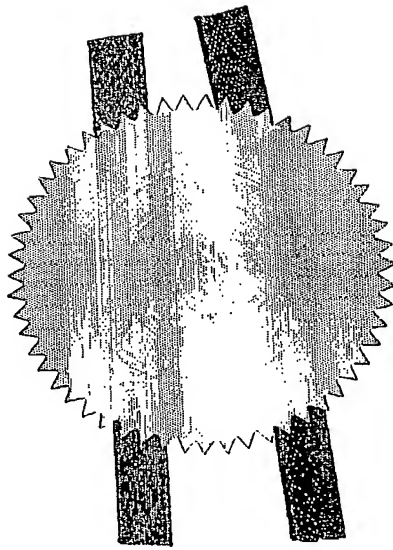
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Applicant(s) /
Proprietor(s) of Patent : MERLIN MD PTE LTD

Title of Invention : IMPLANTABLE MEDICAL DEVICES
HAVING GOOD VISIBILITY AND
MECHANICAL PROPERTIES


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Number of Applicants

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IMPLANTABLE MEDICAL DEVICES HAVING GOOD VISIBILITY AND MECHANICAL PROPERTIES

Field of the Invention

[0001] The present invention generally relates to implantable medical devices including stents which are suitable for intravascular applications, and more particularly to medical devices that are made from platinum:iridium, platinum:tungsten, and other platinum alloys, so that the medical devices have good visibility, excellent mechanical property, and low profile.

Background of the Invention

[0002] Vascular diseases include aneurysms which can rupture and cause hemorrhage, atherosclerosis which can cause the occlusion of blood vessels, vascular malformation and tumors. Vessel occlusion or rupture of an aneurysm within the brain causes of stroke. Tumors fed by intra-cranial arteries can grow within the brain to a point where their mass and size can cause a stroke or the symptoms of stroke, requiring surgery for removal of the tumors or other remedial intervention.

[0003] Occlusion of coronary arteries, for example, is a common cause of heart attack. Diseased and obstructed coronary arteries can restrict the flow of blood in the heart and cause tissue ischemia and necrosis. While the exact etiology of sclerotic cardiovascular disease is still in question, the treatment of narrowed coronary arteries is

more defined. Surgical construction of coronary artery bypass grafts (CABG) is often the method of choice when there are several diseased segments in one or multiple arteries. Conventional open-heart surgery is, of course, very invasive and traumatic for patients undergoing such treatment. Therefore, alternative methods being less traumatic are highly desirable.

[0004] One of the alternative methods is balloon angioplasty that is a technique in which a folded balloon is inserted into a stenosis which occludes or partially occludes an artery and is inflated to open the occluded artery. Another alternative method is atherectomy that is a technique in which occlusive atheromas are cut from the inner surface of the arteries. Both methods suffer from reocclusion with certain percentage of patients.

[0005] A newly preferred therapy for vascular occlusions is placement of an expandable metal wire-frame including stent, within the occluded region of blood vessel to hold it open. The stent is delivered to the desired location within a vascular system by a delivery means, usually a catheter. Advantages of the stent-placement method over conventional vascular surgery include obviating the need for surgically exposing, removing, replacing, or by-passing the defective blood vessel, including heart-lung by-pass, opening the chest, and general anaesthesia.

[0006] When inserted and deployed in a vessel, duct or tract ("vessel") of the body, for example a coronary artery after dilatation of the artery by balloon angioplasty, a stent acts as a prosthesis to maintain the vessel open. The stent usually has an open-ended tubular form with interconnected struts as its sidewall to enable its

expansion from a first outside diameter which is sufficiently small to allow the stent to traverse the vessel to reach a site where it is to be deployed, to a second outside diameter sufficiently large to engage the inner lining of the vessel for retention at the site. A stent is typically delivered in an unexpanded state to a desired location in a body lumen and then expanded. The stent may be expanded via the use of a mechanical device such as a balloon, or the stent may be self-expanding.

[0007] Stents are typically formed from biocompatible metals such as stainless steel, nickel-titanium, cobalt-chromium, tantalum, and the like, which provide sufficient hoop strength to perform the scaffolding function. Furthermore, stents have minimal wall thicknesses in order to minimize blood flow blockage. Stents of various construction have been proposed, including the Palmaz-Schatz® balloon expandable metal stent, the Wallstent self-expanding braided metal stent, the Strecker knitted metal stent, the Instent® coil stent, the Cragg coiled stent and the Gianturco Z stent. However, stents can sometimes cause complications including thrombosis and neointimal hyperplasia, such as by inducement of smooth muscle cell proliferation at the site of implantation of the stent.

[0008] Another factor affecting the choice of stent and stent material is allergic reaction to common stent materials suffered by a statistically significant percentage of the patient population subjected to stenting. These materials include chrome, nickel, and medical 316L stainless steel containing about 16% nickel.

[0009] Another consideration in material selection is the need for an implanting physician to be able to visualize the position of a stent

during implantation to a desired target site in a body, and for purpose of examination from time to time thereafter at the implant site, typically by X-ray fluoroscopy. The wall of the stent must be sufficiently thick, depending on the stent material, not only to withstand the vessel wall recoil that invariably follows deployment at the target site, but to allow the stent to be seen on the fluoroscope. Various materials, such as 316L stainless steel, possess suitable mechanical strength, however the X-ray absorption of the metal is low. The fluoroscopic visibility of stainless steel, for example, in a thickness below 100 μm is very poor because of the limited extinction of x-rays by such a thin metal tube. In addition, increasing the wall thickness of a stent to enhance its radiopacity and recoil resistance makes the stent less flexible. On the other hand, the thinner the stent strut, the less the lumen of the stented vessel is obstructed. Moreover, a thin stent is covered more readily by a neoendothelial build-up. Thus, it is desirable to make the wall of a stent as thin as can be practically achieved, without compromising the stent's strength or visibility.

[0010] It follows that a suitable stent for successful interventional placement should possess features of relatively non-allergenic reaction, good radiopacity, freedom from distortion on magnetic resonance imaging (MRI), flexibility with suitable elasticity to be plastically deformable, strong resistance to vessel recoil, sufficient thinness to minimize obstruction to flow of blood (or other fluid or material in vessels other than the cardiovascular system), and biocompatibility to avoid of vessel re-occlusion. Selection of the

material of which a stent is composed, as well as design of the stent, plays an important role in influencing these features.

[0011] Therefore, there is an imperative need to have implantable medical devices possessing all the desired features. This invention satisfies this need by disclosing the medical devices that are made from platinum:iridium , platinum:tungsten, and other platinum alloys so that the medical devices have good visibility, excellent mechanical properties and low profile.. Other advantages of this invention will be apparent with reference to the detailed description.

Summary of the Invention

[0012] The present invention relates to an implantable medical devices made from a platinum alloy which is selected from the group consisting of platinum:iridium alloy, platinum:tungsten alloy, platinum:rhodium:ruthenium alloy, platinum:rhodium alloy and platinum:nickel alloy. In certain embodiment, the implantable medical devices are stents; wherein the stents comprise a generally tubular structure having an exterior surface defined by a plurality of interconnected struts having interstitial spaces therebetween, said generally tubular structure expandable from a first position to a second position, thereby the lumen of a vascular structure in a body is kept open by the expanded medical devices. In certain embodiments, the implantable medical devices are self-expandable stents. Moreover, the platinum alloys may have a broad range of compositions that are suitable for the fabricating the implantable medical devices claimed in the present application. In addition, the

present invention discloses delivery systems for placing the implantable medical devices of the present invention in a variety of lumens including arteries and veins.

[0013] Accordingly, one object of the present invention is to provide implantable medical devices that have good visibility, excellent mechanical properties and low profile.

[0014] The objects and advantages of the present invention will become apparent from the following detailed description of preferred embodiments thereof in connection with the accompanying drawings.

Brief Description of Drawings

[0015] FIGS. 1A and 1B are two exemplary balloon expandable stents as an illustration of implantable medical devices of the present invention.

[0016] FIG. 2 shows a self-expanding stent as an illustration of implantable medical devices of the present invention.

[0017] FIG. 3 shows a delivery system with a stent expanded onto the balloon in accordance with the present invention.

[0018] FIG. 4 illustrates the anatomy of arteries in the brain showing ischemia and aneurysms.

Detailed Description of the Invention

[0019] The present invention may be understood more readily by reference to the following detailed description of certain embodiments of the invention.

[0020] Throughout this application, where publications are referenced, the disclosures of these publications are hereby incorporated by reference, in their entireties, into this application in order to more fully describe the state of art to which this invention pertains.

[0021] Stents are expandable prostheses employed to maintain vascular and endoluminal ducts or tracts of the human body open and unoccluded, such as a portion of the lumen of a coronary artery after dilatation of the artery by balloon angioplasty. While vascular usage is discussed in detail in this application, it will be understood by those skilled in the art that stents having the characteristics and features of the present invention may be implanted in other ducts or tracts of the human body to keep the lumen open, such as in the cerebral circulation system, tracheo-bronchial system, the biliary hepatic system, the esophageal bowel system, and the urinary tract system. It is also noted that while stents are typical medical devices used for implantation, implantable medical devices that are made from the disclosed alloys of the present invention and used in different applications are not so limited, including vena cava filters, grafts or aneurysm coils.

[0022] A typical stent is a generally tubular structure having an exterior surface defined by a plurality of interconnected struts having

interstitial spaces there between. The generally tubular structure is expandable from a first position, wherein the stent is sized for intravascular insertion, to a second position, wherein at least a portion of the exterior surface of the stent contacts the vessel wall. The expanding of the stent is accommodated by flexing and bending of the interconnected struts throughout the generally tubular structure. It is contemplated that many different stent designs can be produced. An intricate pattern of interconnecting struts can be produced that enable the stent to expand radially when subjected to the appropriate radially directed forces such as are exerted by the inflation of an underlying balloon. A myriad of strut patterns are known for achieving various design goals such as enhancing strength, maximizing the expansion ratio or coverage area, enhancing longitudinal flexibility or longitudinal stability upon expansion, etc. One pattern may be selected over another in an effort to optimize those parameters that are of particular importance for a particular application.

[0023] Now referring to FIGS. 1A and 1B, there are provided two exemplary balloon expandable stent designs. FIG. 1A shows a tubular balloon expandable stent 100 with end markers 103 for further visibility. The stent 100 is composed of stent struts of a ring 101, ring connectors 102, and end markers 103. As shown in FIG. 1A, the stents 100 are made of multiple circumstantial rings 101, where the ring connectors 102 connect two or three adjacent rings 101 to hold the rings in place. For the end markers 103, FIG. 1A shows a "disc" shaped marker. Actually, the shape is not critical so long that the marker can be used to add further visibility to the stents. FIG. 1B shows a tubular balloon expandable stent 104 which is similar to the

stent 100 as shown in FIG. 1A except that the stent 104 comprises of center markers 105, 106. The center markers 105, 106 help to locate an aneurysm opening during an implantation operation. The center markers can be of the same material and shape as the end markers.

[0024] Now referring to FIG. 2, there is provided a self-expanding stent 107 that is made of wires/ribbons. While a self-expanding stent may have many designs, FIG.2 shows the stent 107 having a typical braided pattern 108 with welded ends 109. The stent 107 is so designed that is relatively flexible along its longitudinal axis to facilitate delivery through tortuous body lumens, but that is stiff and stable enough radially in an expanded condition to maintain the patency of a body lumen, such as an artery when implanted therein.

[0025] Referring to FIG. 3, it is shown an expanded tubular stent 112. When the tubular stent 112 is fully expanded to its deployed diameter, the latticework of struts takes on a shape in which adjacent crests undergo wide separation, and portions of the struts take on a transverse, almost fully lateral orientation relative to the longitudinal axis of the stent. Such lateral orientation of a plurality of the struts enables each fully opened cell to contribute to the firm mechanical support offered by the stent in its fully deployed condition, to assure a rigid structure which is highly resistant to recoil of the vessel wall following stent deployment. It bears emphasis, however, that the configuration of this stent structure, while highly desirable, is illustrative only and not essential to the principles of the present invention.

[0026] While a stent may be deployed by radial expansion under outwardly directed radial pressure exerted, for example, by active

inflation of a balloon of a balloon catheter on which the stent is mounted, the present inventors also contemplate that the stent may be self-expandable. In some instances, passive spring characteristics of a preformed elastic (i.e., self-opening) stent serve the purpose. The stent is thus expanded to engage the inner lining or inwardly facing surface of the vessel wall with sufficient resilience to allow some contraction but also with sufficient stiffness to largely resist the natural recoil of the vessel wall.

[0027] Referring still to FIG. 3, the delivery system includes a guide wire lumen 110, a balloon inflating lumen 111, a connector 116, a balloon catheter shaft 113, and ring markers 115 on the catheter shaft 113. The guide wire lumen 110 is used for introducing a guide wire in a balloon catheter, and the balloon inflating lumen 111 for inflating the balloon after the stent to be placed reaches its targeted location. The connector 116 is used for separating the guide wire lumen 110 and the balloon inflating lumen 111. The balloon catheter shaft 113 carries the guide wire lumen 110 and the balloon inflating lumen 111 separately, with a typical length of about 135-170 cm. The ring markers 115 on the catheter shaft 113 is used for showing the start of balloon tapers and the edges of the stent. In FIG. 3, an expanded stent 112 is shown being mounted onto an expanded balloon. The delivery catheter can be essentially a conventional balloon dilatation catheter used for angioplasty procedures. The balloon may be formed of suitable materials such as irradiated polyethylene, polyethylene terephthalate, polyvinylchloride, nylon, and copolymer nylons such as Pebax™. Other polymers may also be used. In order for the stent to remain in place on the balloon during

delivery to the desired site within an artery, the stent is crimped onto the balloon.

[0028] In a preferred embodiment, the delivery of the stent is accomplished in the following manner. The stent is first mounted onto the inflatable balloon on the distal extremity of the delivery catheter. Stent is mechanically crimped onto the exterior of the folded balloon. The catheter/stent assembly is introduced within vasculature through a guiding catheter. A guide wire is disposed across the diseased arterial section and then the catheter/stent assembly is advanced over a guide wire within the artery until the stent is directly under the diseased lining. The balloon of the catheter is expanded, expanding the stent against the artery. The expanded stent serves to hold open the artery after the catheter is withdrawn. Due to the formation of the stent from an elongated tube, the undulating component of the cylindrical elements of the stent is relatively flat in transverse cross-section, so that when the stent is expanded, the cylindrical elements are pressed into the wall of the artery and as a result do not interfere with the blood flow through the artery. The cylindrical elements of the stent which are pressed into the wall of the artery will eventually be covered with endothelial cell growth which further minimizes blood flow interference. Furthermore, the closely spaced cylindrical elements at regular intervals provide uniform support for the wall of the artery, and consequently are well adapted to tack up and hold in place small flaps or dissections in the wall of the artery.

[0029] For resilient or self-expanding prostheses, they can be deployed without dilation balloons. Self-expanding stents can be pre-

selected according to the diameter of the blood vessel or other intended fixation site. While their deployment requires skill in stent positioning, such deployment does not require the additional skill of carefully dilating the balloon to plastically expand the prosthesis to the appropriate diameter. Further, the self-expanding stent remains at least slightly elastically compressed after fixation, and thus has a restoring force which facilitates acute fixation. By contrast, a plastically expanded stent must rely on the restoring force of deformed tissue, or on hooks, barbs, or other independent fixation elements.

[0030] The open reticulated structure of the stent allows for a large portion of the vascular wall to be exposed to blood which can improve the healing and repair of any damaged vessel lining. It is desirable that the stent struts be relatively thin in cross-section to minimize overall profile, yet have enough radial and tensile strength to maintain vessel patency after stent deployment. In order to achieve the radiopaque characteristics desired for clinical procedures, other stent designs must compromise some of the preferred characteristics by increasing the cross-sectional thickness of all the struts, increasing the cross-sectional thickness of some of the struts, or employing other materials for fabrication that fail to have the preferred characteristics of series 300 stainless steels. By fabricating a stent design with the unique alloy described herein, one can optimize the physical and mechanical parameters of the stent design for clinical utility without compromising the desired stent characteristics.

[0031] As discussed above, a stent must have good visibility to assure that its movement and stay can be accurately monitored.

Whether an object is radiopaque will depend on the thickness of the object, the material the object is made of, the attenuation of radiation from surrounding materials, and the energy of the radiation used to image the object. It also follows that for a given object, surrounding material and radiation energy, the material will be radiopaque at thicknesses above a certain threshold and will be nonradiopaque at thicknesses below the threshold. Importantly for the present invention, for commonly used radiation (i.e., radiation energies of about 60 - 120 KeV), 316L is only radiopaque at a stent wall thickness above approximately 0.004 inches in vivo. Thus, stents made of 316L that have wall thicknesses thinner than approximately 0.004 inches generally cannot be successfully imaged in the body using standard radiographic techniques. It is clear that while stainless steel alloys still enjoy its popularity in stent products with thick walls, they fail to meet the challenge of making stents that are strong, thin and good visibility.

[0032] Numerous attempts have been made to improve the visibility of stents made of stainless steel alloys. Some improvement has been achieved by applying a suitable adherent material layer to stent core material of medical grade implantable 316L stainless steel. Layer materials have included gold and certain other noble metals, such as platinum. For example, U.S. Pat. No. 6,623,520 discloses a composite stent having a substrate tube made of stainless steel, a nickel-cobalt-chromium-molybdenum alloy, or chonichrome with at least one metal cladding tube, where the metal cladding tube is made of platinum, gold, tantalum, tungsten, platinum-iridium, palladium, or nickel-titanium; U.S. Pat. No. 6,217,607 discloses a stent with a

three-layer structure comprising a stainless steel layer, gold layer and iridium oxide layer, so that the stent can be used in its stent delivery system that is sized to allow it to traverse small-sized vessels in human body; U.S. Pat. No. 6,527,802 discloses a clad composite stent that comprises a central core and a case surrounding the core, where the core is formed of a radiopaque and relatively ductile material, e.g. tantalum or platinum, and the outer case of a relatively resilient material, e.g. a cobalt/chromium based alloy; and U.S. Pat. No. 6,508,832 discloses a stainless steel stent which is substantially nickel-free and can be embodied in a substrate with one or more metallic cladding overlaying the substrate.

[0033] Such materials typically exhibit much greater radiopacity than does stainless steel. They are also substantially non-allergenic and non-thrombogenic. Such coating may be provided in a very thin layer, to enable the stent wall thickness to be determined almost solely by considerations of mechanical strength. Coatings, however, present a need for absolute adherence to the underlying metal of the stent to avoid cracking or defects in the homogeneous overlying layer, and sufficient resistance to peeling or flaking of the layer during insertion, and especially during expansion of the diameter of the stent as it is being deployed in final position in the artery at the target site, objectives which are not easily achievable.

[0034] Some attempts were also made to incorporate radiopaque elements into stainless steel alloys in order to improve the visibility of stents. For example, WO 02/078764 discloses a stent that is formed from a platinum-stainless steel alloy that has improved radiopacity relative to present utilized stainless steel alloys and

preferably contains from about 2 wt.% to about 50 wt.% platinum, from about 11 wt.% to about 18 wt.% chromium, about 5 wt.% nickel and at least about 15 wt.% iron; and U.S. Pat. No. 6,582,652 discloses an austenitic stainless steel series 300 alloy having improved biocompatible characteristics, where the alloy comprises C, Mn, Si, P, S, Cr, Mo, and platinum or tungsten, wherein the platinum or tungsten is about 5-10 wt.%.

[0035] Moreover, it is known that the disadvantage of reduced mechanical strength of noble metals such as gold or platinum makes them unsuitable if sought to be used alone for application in the human vascular system.

[0036] Nonetheless, the present inventors discovered that platinum:iridium (Pt/Ir), platinum:tungsten (Pt/W) and other platinum alloys possess excellent mechanical properties and good visibility that make them ideal for making implantable medical devices including stents. The present inventors reason that the strength of an alloy is critical for any stents, determining the thickness of the walls of stents. Simply put, the stronger an alloy, the thinner a stent can be made from the alloy. The strength of an alloy can be measured in many different tests, for example, for its ultimate tensile strength under conditions of annealed or stress relieved. The conditions and procedures for the measurement are well known in the art. Table 1 summarizes the ultimate tensile strength under conditions of annealed or stress relieved for Stainless steel 316L-BioDur®, Co-Cr:L605 NickelVac®, platinum, platinum:Iridium-90%:10%, platinum:Iridium-80%:20%, platinum:Iridium-70%:30%, platinum:Tungsten-92%:8%, Platinum:Nickel-90%:10%,

platinum:Rhodium-70%:30%, and platinum:Rhodium:Ruthenium-79%:15%:6%.

[0037] Table 1. Ultimate tensile strength for different alloys.

<u>Alloy</u>	<u>Description</u> <u>Annealed-A</u> <u>Stress Relieved-SR</u>	<u>Ultimate</u> <u>tensile</u> <u>strength-</u> <u>Kpsi-</u> <u>Annealed</u>	<u>Ultimate</u> <u>tensile</u> <u>strength-</u> <u>Kpsi- Stress</u> <u>Relieved</u>
SS: 316L- BioDur™	Tube (A), Wire/Ribbon (SR)	85	150-200*
Co-Cr: L605- NickelVac™	Tube (A), Wire/Ribbon (SR)	150	200-250*
Platinum	Tube (A), Wire/Ribbon (SR)	24	60
Platinum- Iridium-90%: 10%	Tube (A) Wire/Ribbon (SR)	60	150
Platinum- Iridium-80%: 20%	Same as above	120	190
Platinum: Iridium-70%: 30%	Same as above	160	270
Platinum: Tungston-92%: 8% (#479)	Same as above	130	185
Platinum: Nickel-90%: 10%	Same as above	130	200
Platinum: Rhodium-70%: 30%	Same as above	74	160
Platinum: Rhodium: Ruthenium- 79:15: 6	Same as above	95	200

Notes: Source: Johnson Mathey Medical, Sigmund Cohn Corp.
and MatWeb.com

* estimates from various cold worked data sheets

[0038] Annealed tubes are generally used for making balloon expanded stents, where elongation is an important aspect. Typically elongation at break is greater than 20%. Spring like, Stress relieved wires or ribbons can be used to fabricate self-expanding stents. Typical elongation at break is between 1.5-3%. Inventors envision fabricating both types of stents using platinum alloys. Further processing may be needed to make stent surfaces smooth burr free and inert to the blood or body fluids.

[0039] Processing of the alloy is controlled to alleviate concerns over dimensional control of the final thickness of the foil and over maintaining its grain size. Welded tubes made from this alloy are preferably used to fabricate stents, which are made by rolling foil into a tube, laser-welding the seam, then drawing it to the required diameter of the stent. A chemical etching process is used, which requires tubes of extremely consistent wall thickness and grain size in order to produce implant grade medical products.

[0040] No special techniques are required in melting, casting, or working the alloy for fabricating the stent in accordance with the present invention. Induction heating is the preferred method of melting and refining the alloy used in fabricating the present invention stent. Arc melting followed by argon-oxygen decarburization is another method of melting and refining, but other practices can be used. In addition, this alloy can be made using powder metallurgy techniques, if desired. This alloy is also suitable for continuous casting techniques.

[0041] The present stents are typically formed from a cylindrical metal mesh from one of the alloys described herein by using various manufacturing techniques. Alternatively, they can be formed of wire wrapped into a cylindrical shape. However, the present invention is not limited to any particular fabrication method. In preferred embodiments of the present invention, the stent is manufactured from a thin-walled tube, which is then laser cut to provide the desired configuration. The tube may also be chemically etched or electrical discharge machined (EDM) to form the desired configuration. In an alternative embodiment, the stent may be made from a flat pattern which is then formed into a tubular shape by rolling the pattern so as to bring the edges together. The edges may then be joined as by welding or the like to provide a desired tubular configuration. In addition, a thin tubular structure can be made by using a magnetron sputtering as disclosed in U.S. Pat. No. 6,533,905, and the thin tubular structure may then be processed into stents by any known methods.

[0042] There are several manufacturing techniques which can transform a tubular member into a particular stent design: 1) photo-mask and etch techniques as described in U.S. Pat. No. 5,902,475; 2) a laser ablation/etching process disclosed in U.S. Pat. Nos. 6,066,167; 6,056,776; 5,766,238; 5,735,893; 5,514,154 or 5,421,955; and 3) utilizing a laser to directly cut away metal and form the pattern into a tubular member. Any one of these manufacturing examples can be used to produce the present invention stent with the radiopaque alloys.

[0043] In the photo mask and etch process the outer surface of a tubular member is uniformly coated with, e.g., a photosensitive resist. This coated tubular member is then placed in an apparatus designed to rotate the tubular member while the coated tubular member is exposed to a designated pattern of ultraviolet (UV) light. The UV light activates the photosensitive resist causing the areas where UV light is present to expose (cross-link) the photosensitive resist. The photo-sensitive resist forms cross-links where is it exposed to the UV light, thus forming a pattern of hardened and cured polymer which mimics the particular stent design surrounded by uncured polymer. The film is adaptable to virtually an unlimited number of intricate stent designs. The process from the apparatus results in the tubular member having a discrete pattern of exposed photosensitive material with the remaining areas having unexposed photosensitive resist.

[0044] The exposed tubular member is immersed in a resist developer for a specified period of time. The developer removes the relatively soft, uncured photosensitive resist polymer and leaves behind the cured photosensitive resist which mimics the stent pattern. Thereafter, excess developer is removed from the tubular member by rinsing with an appropriate solvent. At this time, the entire tubular member is incubated for a specified period of time, allowing the remaining photosensitive resist polymer to fully cure and bond to the surface of the processed tubular member.

[0045] The processed tubular member is then exposed to an electrochemical etching process which removes uncovered metal from the tubular member, resulting in the final tubular member or stent configuration.

[0046] In an example of the laser/etching process, a tubular member is coated with a resist and placed in a rotatable collet fixture of a machine-controlled apparatus for positioning the tubular member relative to a laser. Then, according to the machine coded instructions, the tubing is rotated and moved longitudinally relative to the laser which is also machine controlled wherein the laser selectively removes the resistant coating on the tubular member by ablation. A stent pattern is formed on the surface of the tubular member that is created by a subsequent chemical etching process.

[0047] In an example of the direct laser method, a tubular member is placed in a collet fixture of a machine-controlled apparatus for positioning the tubular member relative to a laser. Then, according to the machine coded instructions, the tubing is rotated and moved longitudinally relative to the laser which is also machine controlled wherein the laser selectively ablates and removes metal forming the stent pattern.

[0048] The presence of a stent in a vessel tends to promote thrombus formation as blood flows through the vessel, which results in an acute blockage. In addition, as the outward facing surface of the stent in contact or engagement with the inner lining of the vessel, tissue irritation can exacerbate restenosis attributable to hyperplasia. The thrombosis and occlusion caused by the placement of the stent may be reduced or even eliminated by proper modification of the surface of the stent.

[0049] Surface modification of the stent to apply a desired coating such as iridium oxide or titanium nitrate may be achieved by vapor deposition or plasma deposition, or other conventional

methods. Such modification may be used to give the stent a rough surface. Alternatively, the surface may be passivated only, by oxidation of the iridium for reduced immunoresponse and less throubogenicity. Other surface modification may include Ion Implantation process which forms a barrier to metal such as nickel to leach out.

[0050] In the evolution of stents, there have been developments in the field of stents coated with a layer of polymers. The polymeric materials are typically capable of absorbing and releasing therapeutic drugs. Examples of such stents are disclosed in U.S. Pat. No. 5,443,358 to Eury; U.S. Pat. No. 5,632,840 to Campbell; U.S. Pat. No. 5,843,172 to Yan; and U.S. Ser. No. 08/837,993, filed Apr. 15, 1997, by Yan.

[0051] Stents of the present invention may be coated with one or more layers (coatings). The external surfaces and intratubular surfaces may have different coatings. The coatings may incorporate any desired substances including therapeutic substances, alone or in a carrier, so that the substances are released over time after implantation. The coatings usually employ polymers that include polycarboxylic acids; cellulosic polymers including cellulose acetate and cellulose nitrate; gelatin; polyvinylpyrrolidone; crosslinked polyvinylpyrrolidone; polyanhydrides including maleic anhydride polymers; polyamides; polyvinyl alcohols; copolymers of vinyl monomers such as EVA; polyvinyl ethers; polyvinyl aromatics; polyethylene oxides; polyesters including polyethylene terephthalate; polyacrylamides; polyethers; polyether sulfone; polycarbonate; polyalkylenes including polypropylene, polyethylene and high

molecular weight polyethylene; halogenated polyalkylenes including polytetrafluoroethylene; polyurethanes; polyorthoesters; silicones; siloxane polymers; polylactic acid; polyglycolic acid; polycaprolactone; polyhydroxybutyrate valerate and blends and copolymers thereof; polypeptides; proteins including fibrin, collagen and derivatives thereof; glycosaminoglycans; polysaccharides such as celluloses, starches, dextrans, alginates and derivatives; hyaluronic acid; and squalene emulsions.

[0052] Therapeutic substances which can be delivered from stents of the present invention include anti-thrombogenic agents such as heparin, heparin derivatives, urokinase, and PPACK (dextrophenylalanine proline arginine chloromethylketone); anti-proliferative agents such as enoxaprin, angiopeptin, or monoclonal antibodies capable of blocking smooth muscle cell proliferation, hirudin, and acetylsalicylic acid; anti-inflammatory agents such as dexamethasone, prednisolone, corticosterone, budesonide, estrogen, sulfasalazine, and mesalamine; antineoplastic/antiproliferative/anti-miotic agents such as paclitaxel, 5-fluorouracil, cisplatin, vinblastine, vincristine, epothilones, endostatin, angiostatin and thymidine kinase inhibitors; anesthetic agents such as lidocaine, bupivacaine, and ropivacaine; anticoagulants such as D-Phe-Pro-Arg chloromethyl keton, an RGD peptide-containing compound, heparin, antithrombin compounds, platelet receptor antagonists, antithrombin anticodies, anti-platelet receptor antibodies, aspirin, prostaglandin inhibitors, platelet inhibitors and tick antiplatelet peptides; vascular cell growth promotors such as growth factor inhibitors, growth factor receptor antagonists, transcriptional activators, and translational promotors;

vascular cell growth inhibitors such as growth factor inhibitors, growth factor receptor antagonists, transcriptional repressors, translational repressors, replication inhibitors, inhibitory antibodies, antibodies directed against growth factors, bifunctional molecules consisting of a growth factor and a cytotoxin, bifunctional molecules consisting of an antibody and a cytotoxin; cholesterol-lowering agents; vasodilating agents; and agents which interfere with endogenous vasoactive mechanisms; anti-sense DNA and RNA; DNA coding for anti-sense RNA; tRNA or rRNA to replace defective or deficient endogenous molecules; angiogenic factors including growth factors such as acidic and basic fibroblast growth factors, vascular endothelial growth factor, epidermal growth factor, transforming growth factor α and β , platelet-derived endothelial growth factor, platelet-derived growth factor, tumor necrosis factor α , hepatocyte growth factor and insulin like growth factor; cell cycle inhibitors including CD inhibitors; thymidine kinase ("TK") and other agents useful for interfering with cell proliferation; the family of bone morphogenic proteins ("BMP's"); and BMP-2, BMP-3, BMP-4, BMP-5, BMP-6 (Vgr- 1), BMP-7 (OP- 1), BMP-8, BMP-9, BMP-10, BMP-11, BMP-12, BMP-13, BMP-14, BMP-15, and BMP-16. Currently preferred BMP's are any of BMP-2, BMP-3, BMP BMP-5, BMP-6 and BMP. These dimeric proteins can be provided as homodimers, heterodimers, or combinations thereof, alone or together with other molecules. Alternatively or, in addition, molecules capable of inducing an upstream or downstream effect of a BMP can be provided. Such molecules include any of the "hedgehog" proteins, or the DNA's encoding them.

[0053] Stents or prostheses have been largely used in vascular structures including arteries and veins. Aside from vascular usage, other ducts or tracts of the human body in which a stent might be installed to maintain an open lumen include the tracheo-bronchial system, the biliary hepatic system, the esophageal bowel system, and the urinary tract. Many of the same requirements are found in these other endoluminal usages of stents.

[0054] Stents are used in many ways. For instance, stents have been used after atherectomy or standard balloon angioplasty to maintain acute and long-term patency of the vessel. Stents have also been used to overlies an aortic dissecting aneurysm, tack dissections to the vessel wall, eliminate the risk of occlusion caused by flaps resulting from the intimal tears associated with primary interventional procedure, or prevent elastic recoil of the vessel. Stents may be utilized in by-pass grafts as well, to maintain vessel patency. Stents can also be used to reinforce collapsing structures in the respiratory, biliary, urological, and other tracts.

[0055] The stents of the present invention are perfectly suitable for placement in small vascular structures such as of the brain. FIG. 4 shows a diagram of ICA and Circle of Willis (CW) arteries. As can be seen from FIG. 4, the internal carotid artery (ICA) 117 supplies blood to arteries such as middle cerebral artery (MCA), and Circle of Willis. Also seen in Fig 4 is vertebral arteries (VA) supplying blood to basilar (BA) and Intracranial arteries through Circle of Willis. Ischemic disease is shown in VA, ICA, BA and MCA. Aneurysms are shown on CW, and ICA.

[0056] Access to small occluded arteries of the brain to allow adequate blood flow (Ischemic) or repair ruptured aneurysm is highly desirable for treating millions of people who suffer from stroke each year. One of the technical prerequisites for successful treatment in these respects is the availability of a stent, and related delivery system, which is sufficiently small and thin that it can navigate and be and deployed in these tiny vessels without occluding or damaging the lumen thereof. It is also essential that the stent be highly visible during and after implantation to enable proper deployment and aftercare by the physician. The latter attribute is especially important for treatment of intracerebral arteries, because of the obstacle to x-rays presented by the skull which makes precise visualization of a small thin stent extremely difficult. The stent should, therefore, be sufficiently radiopaque without need for its struts to be made so thick that the stent itself creates an unacceptable obstruction of the lumen of the vessel or too stiff to navigate through tortuous intracranial anatomy. Another prerequisite of a successful treatment of these extremely small diameter vessels is that the stent delivery system should be highly flexible to allow it to be advanced along the anatomy of the cerebral circulation. In addition, the total stent delivery system must be of extremely small profile, to treat diseased intra-cranial arteries generally ranging from 1.5mm to 5mm.

[0057] The stents made from platinum:iridium, platinum:tungsten and other platinum alloys are strong with a very thin walls. In certain embodiments, the walls of stents can be thinner than 0.0028". In certain embodiments, the walls of stents can be about 0.0012" to 0.0028". Therefore, the stents and delivery

systems in accordance with the present invention satisfy the needs to use stents in the cerebral circulation.

[0058] From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

What is claimed is:

1. An implantable medical devices made from a platinum alloy which is selected from the group consisting of platinum:iridium alloy, platinum:tungsten alloy, platinum:rhodium:ruthenium alloy, platinum:rhodium alloy and platinum:nickel alloy.
2. The implantable medical devices of claim 1, wherein the medical devices are stents; wherein the stents comprise a generally tubular structure having an exterior surface defined by a plurality of interconnected struts having interstitial spaces therebetween, said generally tubular structure expandable from a first position to a second position, thereby the lumen of a vascular structure in a body is kept open by the expanded medical devices.
3. The implantable medical devices of claim 2, wherein the stents are self-expandable stents.
4. The implantable medical devices of any of claims 1-3, wherein the platinum:iridium alloy has a composition of about 60-90 % of platinum and 10-40% of iridium.
5. The implantable medical devices of claim 4, wherein the platinum:iridium alloy has a preferred composition of about 70-90% of platinum and 10-30% iridium.

6. The implantable medical devices of claim 5, wherein the platinum:iridium alloy has a preferred composition of about 70-80% of platinum and 20-30% iridium.
7. The implantable medical devices of any of claims 1-3, wherein the platinum:tungsten alloy has a preferred composition of about 85-95% of platinum and 5-15% of tungsten.
8. The implantable medical devices of claim 7, wherein the platinum:tungsten alloy has a preferred composition of about 90-95% of platinum and 5-10% of tungsten.
9. The implantable medical devices of any of claims 1-3, wherein the platinum:rhodium:ruthenium alloy has a preferred composition of about 70-85% of platinum, 10-20% of rhodium and 3-10% of ruthenium.
10. The implantable medical devices of claim 9, wherein the platinum:rhodium:ruthenium alloy has a preferred composition of about 75-80% of platinum, 12-18% of rhodium and 5-10% of ruthenium.
11. The implantable medical devices of any of claims 1-3, wherein the platinum:rhodium alloy has a preferred composition of about 60-80% of platinum and 20-40% of rhodium.

12. The implantable medical devices of claim 11, wherein the platinum:rhodium alloy has a preferred composition of about 65-75% of platinum and 25-35% of rhodium.

13. The implantable medical devices of any of claims 1-3, wherein the platinum:nickel alloy has a preferred composition of about 80-90% of platinum and 10-20% of nickel.

14. The implantable medical devices of claim 13, wherein the platinum:nickel alloy has a preferred composition of about 85-90% of platinum and 10-15% of nickel.

15. The implantable medical devices of any of claims 1-14, wherein the wall thickness of the implantable medical devices is less than 0.0035".

16. The implantable medical devices of any of claims 1-15, wherein the surfaces of the implantable medical devices may be modified by passive coatings.

17. The implantable medical devices of any of claims 1-16, wherein the medical devices are coated with external layer containing a pharmaceutically effect amount of therapeutic elements.

18. A delivery system for placing an implantable medical device of any of claims 1-17 within a lumen of a body, wherein the implantable medical devices are expandable by balloon inflation, comprising a

balloon delivering catheter and expandable implantable medical device, wherein the expandable medical device is mounted onto the balloon of the delivering catheter.

19. A delivery system for placing an implantable medical device of any of claims 1-17 within a lumen of a body, wherein the implantable medical devices are self-expandable, comprising a delivering catheter and the self-expandable implantable medical device, wherein the medical device is mounted onto the distal portion of the delivering catheter.

IMPLANTABLE MEDICAL DEVICES HAVING GOOD VISIBILITY AND MECHANICAL PROPERTIES

ABSTRACT

The present invention relates to an implantable medical devices made from a platinum alloy which is selected from the group consisting of platinum:iridium alloy, platinum:tungsten alloy, platinum:rhodium:ruthenium alloy, platinum:rhodium alloy and platinum:nickel alloy. The implantable medical devices are stents; wherein the stents comprise a generally tubular structure having an exterior surface defined by a plurality of interconnected struts having interstitial spaces therebetween, said generally tubular structure expandable from a first position to a second position, thereby the lumen of a vascular structure in a body is kept open by the expanded medical devices. The implantable medical devices are also self-expandable stents. In addition, the present invention discloses delivery systems for placing the impantable medical devices of the present invention in a variety of lumens including arteries and veins.

FIG. 4

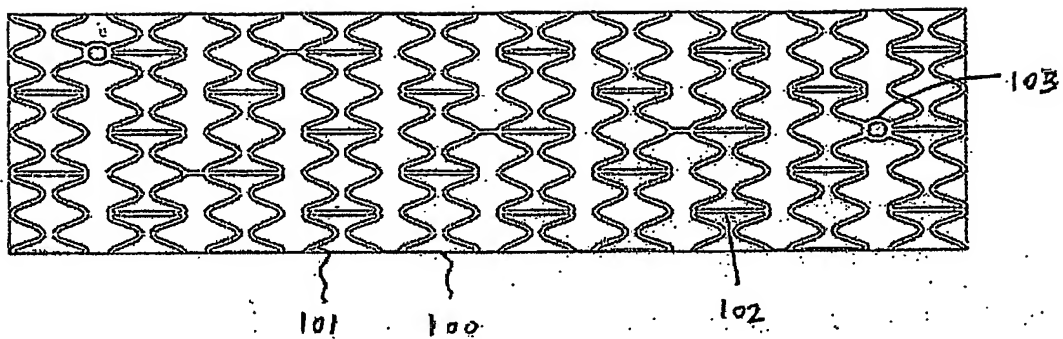


FIG. 1A

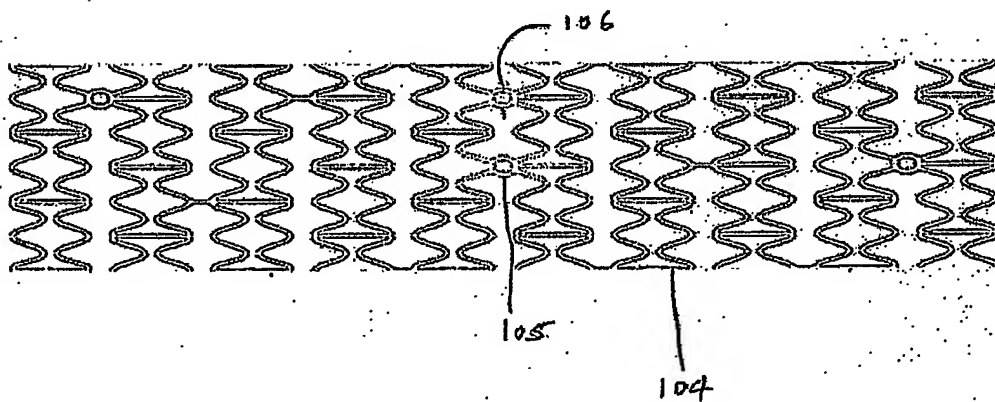


FIG. 1B

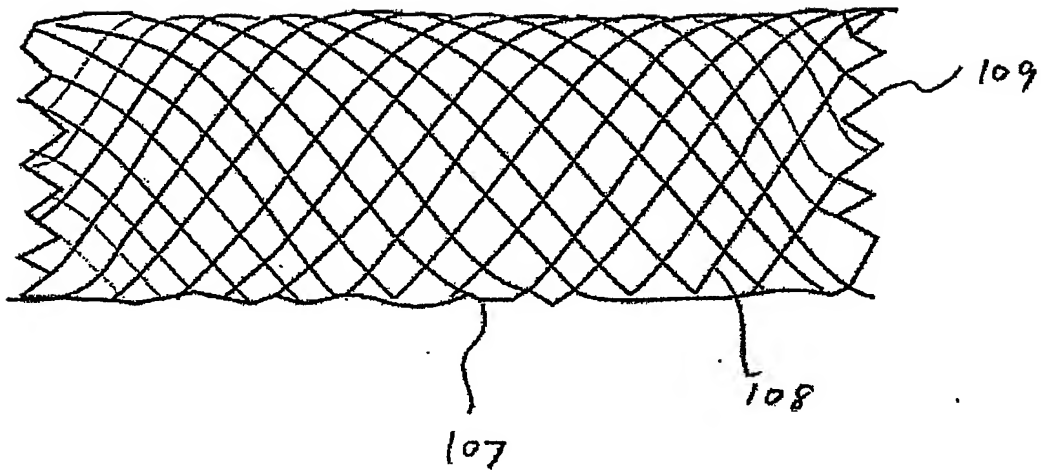


FIG. 2

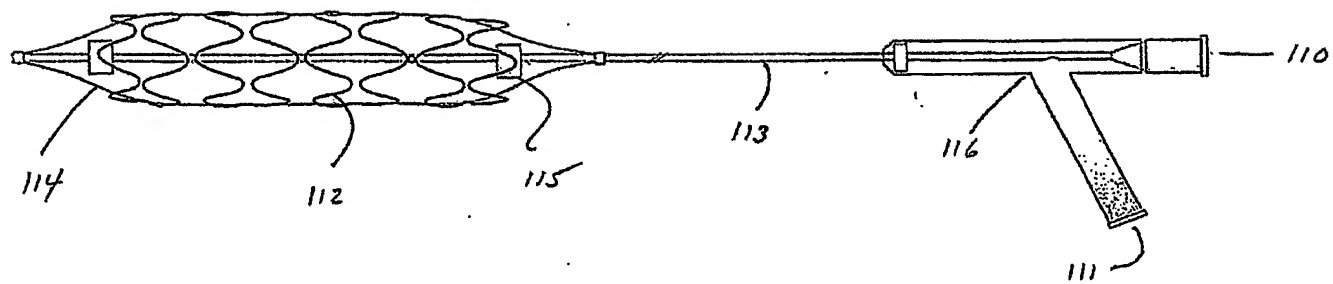
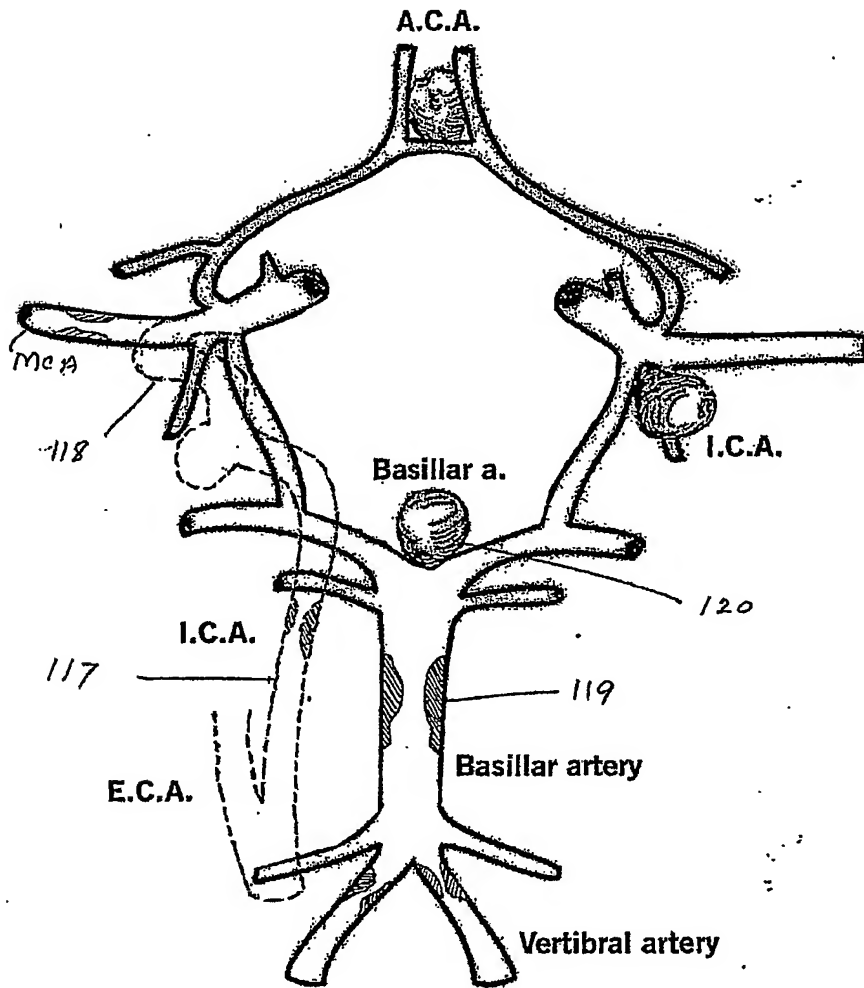


FIG. 3



ICA & Circle of Willis Arteries

FIG. 4

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